

and metabolic functions, and circulating inflammatory markers might help to better characterise these patients.

### Diagnosis of COPD

J. Vestbo

*Hvidovre Hospital & University of Copenhagen, DK, and Wythenshawe Hospital & University of Manchester, UK*  
E-mail address: Jorgen.Vestbo@manchester.ac.uk

The diagnosis of COPD relies on the demonstration of fixed airflow limitation in the absence of less frequent diseases causing airways obstruction. Guidelines have for decades used the ratio of FEV<sub>1</sub>/VC or FEV<sub>1</sub>/FVC as the measurements of choice; this has rarely been the cause of debate whereas the cut-off values for the ratio have been intensely debated. The fixed ratio of 0.7 causes under-diagnosis of COPD in younger adults and over-diagnosis in the elderly whereas the use of lower limit of normal presumes that less than 5% of elderly asymptomatic smokers can have COPD as 'normality' is defined according to statistics only.

More importantly, however, the current diagnostic guidance does not take into account that we define COPD as 1) a disease characterised by an abnormal inflammatory response, 2) a disease with a frequently occurring extrapulmonary component - and 3) that we know that one of the main subtypes of COPD, emphysema, often does not lead to airflow limitation in its earliest stages. We will need to decide whether we want to keep our simple diagnostic criteria and subsequently try to describe the individual patient's features by "sub-grouping" COPD or whether our diagnostic criteria should mirror how we define the disease.

### Disease modification in COPD – impacting the clinical course

P. Lange

*Department of Cardiology and Respiratory Medicine, Hvidovre Hospital, University of Copenhagen, Denmark*  
E-mail address: plange@dadlnet.dk

The most recent definition of COPD clearly states that the disease is both preventable and treatable. The knowledge on interventions that may improve the clinical course of COPD is constantly expanding and the COPD patients of today are facing a totally different approach from the health professionals compared to the situation 20 years ago. This means that the clinical course of the disease need no longer result in a continuing decline of lung function, repeated exacerbations and development of respiratory failure. Whereas smoking cessation in the early stage of COPD and long term oxygen treatment in the end-stage disease were in the past thought to be the only two modalities affecting the long term clinical course of the disease, it is now documented that also pharmacological treatment with

long acting antimuscarinic agents, long acting beta-2-agonists and inhaled corticosteroids, rehabilitation comprising physical exercise and immunisation against influenza affects the long term prognosis and improves the health related quality of life of the patients. Also the treatment of acute exacerbations with non-invasive ventilation has revolutionised the clinical practice by reducing both mortality and the need for intubation.

In order to implement these options with success, the timing of intervention is essential. In this context the more widespread use of spirometry, assessment of the severity of dyspnea and identification of patients with repeated exacerbation is mandatory. The pulmonary community has a major obligation in assuring that the knowledge from the successful controlled trials will be implemented in the clinical practice.

### ABSTRACTS - OTHER LECTURERS

#### Exhaled NO and systemic inflammation biomarkers in COPD - a longitudinal study

N.B. Roberts, J. Vestbo and T.A. Gerds

*Pulmonary Cardiology Department of Hvidovre Hospital, Department of Biostatistics, Copenhagen University, Denmark*  
E-mail address: nassim\_dk@yahoo.com

The usefulness of exhaled nitric oxide (eNO) measurement is still controversial in chronic obstructive pulmonary disease (COPD). However, modelling measurements of eNO from multiple flows may provide measures of parenchymal and airway inflammation and could potentially be used to monitor inflammation in COPD. In my PhD study I will investigate any possible correlation between local inflammation and systemic inflammation in COPD patients and relate it to presence/development of cardiac disease.

Ninety one (91) COPD patients recruited in the ECLIPSE study with FEV<sub>1</sub> ranging from 17-77% have been seen every three months in the first year and every six months in the following eighteen month period. I aim to use two compartment nonlinear modelling of multiple flow rates eNO at 10, 30, 50, 100 and 200 mL·s<sup>-1</sup>, but currently only raw eNOs are available and eNO<sub>50</sub> is used to indicate airway inflammation. The following biochemical markers of inflammation in serum are used: IL-6, IL-8, TNF<sub>α</sub>, Clara cell secretory protein-16 (CC-16), and Surfactant Protein D (SPD).

Neither eNO<sub>50</sub> nor any of the systemic markers varied according to age, gender or GOLD stage except IL6 which increased by age. There was no correlation between eNO<sub>50</sub> and any of the systemic markers. There was an association between TNF<sub>α</sub> and PARC (r=.26, p=.01) but no other inter-relations between systemic markers. IL-6 was significantly elevated in subjects with ischemic heart disease (7.27 vs 2.13 pg/mL, p<.001) as was CC-16 (6.17 vs. 4.86 ng/mL, p=.03), none of the others markers were related to heart disease at baseline.

Future analyses of my study cohort can hopefully provide more data on the association between local and systemic inflammation and cardiac comorbidities in COPD.

#### **Intracellular antioxidant enzyme difference in COPD reflects age-related declines in function, rather than disease state**

**A.F. Behndig, A. Blomberg, E. Roos-Engstrand and I.S. Mudway**

*Department of Respiratory Medicine and Allergy, University Hospital Umeå, Sweden and Lung Biology, School of Biomedical and Health Sciences, Franklin-Wilkins Building, King's College London, UK  
E-mail address: Annelie.behndig@lung.umu.se*

**Background:** Numerous studies have demonstrated evidence of oxidative stress in COPD, in both respiratory tract lining fluids and biopsies. Antioxidant response in airway inflammatory cells to a pro-oxidative environment is however poorly understood. We have previously demonstrated an enhanced antioxidant enzyme activity in macrophages from asthmatics. This study was performed to assess whether a similar adaptation in intra-cellular antioxidants occurred in subjects with COPD. The activities of enzymatic antioxidants were examined in alveolar mixed cell populations and compared to healthy age-matched controls (ACs) and young adults, to permit the relative contributions of disease state and natural ageing to be disentangled.

**Methods:** Airway leukocytes were obtained by bronchoscopy-based lavage and cellular activities of Cu,Zn superoxide dismutase (SOD1), glutathione peroxidase (GPx), catalase (CAT) and glutathione reductase (GSSG-red) were determined. In addition, cellular glutathione and glutathione disulphide concentrations were quantified to determine cellular redox status.

**Results:** No differences in the activity of the major enzymatic antioxidants or intra-cellular GSH concentration were observed between COPD patients and ACs. In contrast, significantly reduced SOD1 ( $p<0.001$ ), GPx ( $p=0.04$ ) and GSSG-red ( $p=0.01$ ) activities were observed in the ACs relative to the young adult group. In contrast, catalase activity was elevated in the ACs ( $p=0.001$ ), but again with no further enhancement in the COPD group.

**Conclusion:** These data demonstrate a loss of adaptive plasticity associated with ageing, rather than a COPD-specific down regulation of antioxidant defences. These data do however highlight that in COPD, unlike asthma, the imposition of oxidative stress does not induce protective adaptations, implying a greater sensitivity to oxidant injury *in vivo*.

#### **Neurotrophins in COPD**

**C. Dagnell<sup>1</sup>, M. Mikko<sup>1</sup>, M. Löfdahl<sup>1</sup>, E. Roos-Engstrand<sup>2</sup>, A. Blomberg<sup>2</sup>, M. Sköld<sup>1</sup> and C.O. Höglund<sup>1,3</sup>**

*<sup>1</sup>Department of Medicine Solna, Respiratory Medicine Unit, Karolinska Institutet and Karolinska University Hospital Solna, Stockholm, Sweden*

*<sup>2</sup>Department of Respiratory Medicine and Allergy, University Hospital, Umeå, Sweden*

*<sup>3</sup>Department of Physiology and Pharmacology, Karolinska Institutet, Stockholm, Sweden*

*E-mail address: charlotta.dagnell@ki.se*

Nerve growth factor (NGF) and neurotrophin-3 (NT-3) belong to the neurotrophin family and are important growth- and survival factors for neurons. Lately, they have also been shown to be potent inflammatory mediators as well as factors promoting tissue repair processes. Increased levels of neurotrophins have previously been shown in the airways of patients with asthma and sarcoidosis.

In this study we investigated the levels of neurotrophins in the airways of patients with moderate to severe COPD ( $n=25$ ), healthy non-smokers ( $n=12$ ) and asymptomatic smokers ( $n=16$ ). We found decreased levels of NGF and NT-3 in bronchoalveolar lavage fluid (BALF) in COPD patients and asymptomatic smokers as compared to healthy non-smokers. These findings suggest that smoking per se decreases the release of neurotrophins in the airways. Structural cells, such as epithelial cells and fibroblasts, are known sources of neurotrophins. We found that NGF secretion was decreased from cultured human lung fibroblasts exposed to cigarette smoke extract.

These results indicate that smoking have inhibitory effects on neurotrophin secretion in the airways. The functional consequence of lower levels of neurotrophins in the airways of smokers and COPD patients is still unknown and further studies are required to elucidate the role of neurotrophins in inflammatory pulmonary diseases.

#### **Non-invasive markers of airway inflammation in COPD**

**L. Lehtimäki, H. Kankaanranta, I. Annala, T. Aine, S. Saarelainen and E. Moilanen**

*Department of Respiratory Medicine, Tampere University Hospital, Medical School, University of Tampere, Tampere, Finland*

*E-mail address: lauri.lehtimaki@uta.fi*

Chronic airway inflammation is a key feature in the pathogenesis of COPD, and inhaled corticosteroids (ICS) are widely used to alleviate airway inflammation in COPD. We tested if non-invasive markers of airway inflammation are related to lung function in COPD, or if these markers can predict responsiveness to ICS.